

PUBLIC HEALTH SERVICE

BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH

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Professor Joshua Lederberg Department of Genetics Stanford University Palo Alto, California

Dear Josh:

Thanks for calling me last week, and I am sorry to have pressed you. I'd have been willing to wait on your convenience, but our director was not. The approximate cost of the call is enclosed.

I know my hypothesis that evolution toward complexity by selection could occur without polymeric molecules as genes seems irrational. I have already all I want to on the subject, however, and will work now toward demonstrating it experimentally. I realize that it will probably be a lifelong program, and that even then I may fail. Such a failure would not, as I see thingsnow, diminish my conviction that the reasoning is valid, or that these phenomena probably controlled a very important phase in the transition from lifeless to living systems.

The finding of one autocatalytic synthesis (not a degradation or hydrolysis) would not, I understand, put me in business, but it would answer the protests of some people that such systems do not exist at all. The next step would be to find some more systems of the same sort, and finally I would try to show that, when several such systems coexist, the products are likely to be more complex than those of all the component catalysts acting singly. If complex products accumulate, so will the number of catalysts, and competition would favor the most efficient systems and those that could best cooperate with the others. This, I believe, could gradually convert the mixture to a metabolizing system, capable of carrying out coordinated syntheses under catalysis. I wouldn't expect every to obtain more than the earliest indications of such an evolution.

On citation indexes, I have gradually come into complete agreement with the views expressed in your letter to me of last October. I favor avoidance of any selective extraction of citations, but if a pilot study is required it might usefully start from journals on general science together with all those in some specialized area, like genetics. The resulting index would list all articles cited in these journals regardless of date, source or subject. These citations wouldn't all have to be published, but could be saved for use in a later, complete index. I wrote to the NSF that, if they approved Garfield's application, I as a member of the advisory committee would favor revision of the design in this direction.

Sincerely yours,